

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number  
**WO 2004/092170 A3**

(51) International Patent Classification: C07D 487/04,  
519/00, A61K 31/53, 31/519, A61P 25/06, 25/16, 25/24,  
25/28

(21) International Application Number:  
PCT/US2004/011005

(22) International Filing Date: 9 April 2004 (09.04.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/461,356 9 April 2003 (09.04.2003) US

(71) Applicant (for all designated States except US): BIOGEN IDEC MA INC. [US/US]; 14 Cambridge Center, Cambridge, MA 02142 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): VU, Chi [US/US]; 79 Bay State Road, Arlington, MA 02474 (US). PETTER, Russell C. [US/US]; 343 Hudson Road, Stow, MA 01775 (US). KUMARAVEL, Gnanasambandam [IN/US]; 10 Perham Circle, Westford, MA 01886 (US).

(74) Agent: LINKKILA, Timothy P.; BIOGEN IDEC MA INC., 14 Cambridge Center, Cambridge, MA 02142 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

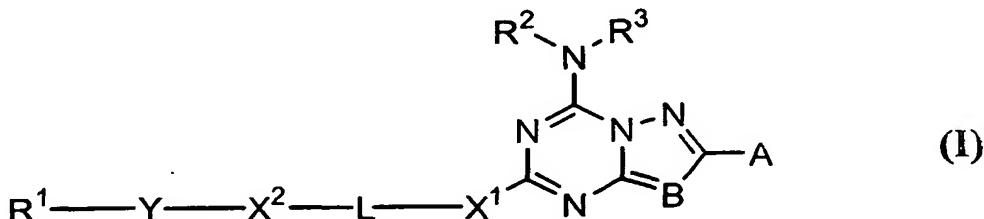
Published:

— with international search report

(88) Date of publication of the international search report:  
31 March 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: TRIAZOLOTRIAZINES AND PYRAZOLOTRIAZINES USEFUL AS A2A ADENOSINE RECEPTOR ANTAGONISTS



WO 2004/092170 A3

(57) Abstract: The invention is based on the discovery that compounds of formula (I) possess unexpectedly high affinity for the A<sub>2a</sub> adenosine receptor, and can be useful as antagonists thereof for preventing and/or treating numerous diseases, including Parkinson's disease. In one embodiment, the invention features a compound of formula I: (I)

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/011005

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D487/04 C07D519/00 A61K31/53 A61K31/519 A61P25/06  
A61P25/16 A61P25/24 A61P25/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 515 107 A (ICI PLC) 25 November 1992 (1992-11-25)  examples page 7, paragraph 2; claims 1-10	1, 25-32, 36, 40, 42, 44, 46-51
X	EP 0 459 702 A (ICI PLC) 4 December 1991 (1991-12-04)  examples page P, line 41 - line 44; claims 1-16	1, 25-32, 36, 40, 42, 44, 46-51

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

8 October 2004

Date of mailing of the international search report

11.01.2005

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Stroeter, T

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/011005

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FRANCIS J E ET AL: "STRUCTURE-ACTIVITY PROFILE OF A SERIES OF NOVEL TRIAZOLOQUINAZOLINE ADENOSINE ANTAGONISTS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 31, 1988, pages 1014-1020, XP002136848 ISSN: 0022-2623 (whole left-hand col. of page 1018) page 1018, paragraphs 1,2; figures 1,2	1,25-32, 36,40, 42,44, 46-51
A	EP 0 667 349 A (KYOWA HAKKO KOGYO KK) 16 August 1995 (1995-08-16)	1,25-32, 36,40, 42,44, 46-51
	compound 4	
A	FR 2 230 366 A (SANDOZ SA) 20 December 1974 (1974-12-20)	1,25-32, 36,40, 42,44, 46-51
	the whole document	

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/011005

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 40-51 because they relate to subject matter not required to be searched by this Authority, namely:  

Although claims 40 to 51 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1, 25-32, 36, 40, 42, 44, 46-51 (all part)

#### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 25-32, 36, 40, 42, 44, 46-51 (each partial)

compounds (and subject-matter referring to these compounds) of formula (I) wherein L = phenyl (first structure)  
---

2. claims: 1, 28-32, 40, 42, 44, 46-51(each partial)

compounds (and subject-matter referring to these compounds) of formula (I) wherein L = cycloalkyl (2nd structure)  
---

3. claims: 1, 28-32, 40, 42, 44, 46-51 (each partial) and 2-24, 32-35, 37-39 (each complete)

compounds (and subject-matter referring to these compounds) of formula (I) wherein L = saturated N-heteromonocycle (3rd to 12th structure)  
---

4. claims: 1, 25-32, 40, 42, 44, 46-51 (each partial)

compounds (and subject-matter referring to these compounds) of formula (I) not yet comprised by groups 1-3 wherein L bond (and X1= alkynylen)  
---

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No PCT/US2004/011005	
---	--

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
EP 0515107	A 25-11-1992		AU 654010 B2 AU 1709392 A CA 2069455 A1 CS 9201533 A3 EP 0515107 A2 FI 922340 A HU 62898 A2 IE 921655 A1 JP 5155887 A MX 9202442 A1 NO 922028 A NZ 242865 A US 5290776 A ZA 9203767 A	20-10-1994 26-11-1992 24-11-1992 16-12-1992 25-11-1992 24-11-1992 28-06-1993 02-12-1992 22-06-1993 01-11-1992 24-11-1992 26-05-1995 01-03-1994 28-04-1993
EP 0459702	A 04-12-1991		AU 642494 B2 AU 7734891 A CA 2043424 A1 CS 9101595 A3 EP 0459702 A1 FI 912563 A GB 2244487 A ,B HU 61311 A2 IE 911818 A1 IL 98316 A JP 2504879 B2 JP 5097855 A NO 912051 A ,B, NZ 238288 A OA 9358 A PL 167014 B1 PT 97776 A RO 109542 B1 US 5356894 A US 5270311 A ZA 9104094 A AP 248 A CN 1056879 A	21-10-1993 05-12-1991 30-11-1991 15-01-1992 04-12-1991 30-11-1991 04-12-1991 28-12-1992 04-12-1991 26-05-1995 05-06-1996 20-04-1993 02-12-1991 27-07-1993 15-09-1992 31-07-1995 31-03-1992 30-03-1995 18-10-1994 14-12-1993 26-02-1992 16-03-1993 11-12-1991
EP 0667349	A 16-08-1995		AT 198890 T AU 7546794 A DE 69426620 D1 DE 69426620 T2 EP 0667349 A1 US 5789407 A CA 2148502 A1 ES 2156901 T3 WO 9507282 A1	15-02-2001 27-03-1995 01-03-2001 21-06-2001 16-08-1995 04-08-1998 16-03-1995 01-08-2001 16-03-1995
FR 2230366	A 20-12-1974		CH 581137 A5 AU 6925974 A DD 113907 A5 DE 2424334 A1 FI 146174 A FR 2230366 A1 JP 50019769 A NL 7406641 A BE 815405 A1	29-10-1976 27-11-1975 05-07-1975 19-12-1974 23-11-1974 20-12-1974 01-03-1975 26-11-1974 22-11-1974

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/US2004/011005

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR 2230366	A	ES 426482 A1 ZA 7403316 A	01-09-1976 28-01-1976